and optimal treatment. METHODS: Patients with molecularly-profiled HGG (Caris Life Sciences; Phoenix, AZ) with LMD at two institutions were included. Medical records were reviewed for clinicopathological characteristics, treatment, and outcome. Kaplan-Meier estimates of patient survival were performed on censored data using Cox's proportional hazard model. RESULTS: 43 patients (male: 33, female: 10; median age: 56 years) were identified, comprising 41 grade 4 (glioblastoma: 38; gliosarcoma: 2; H3K27M diffuse midline glioma: 1) and 2 grade 3 tumors (astrocytoma: 1; pleomorphic xanthoastrocytoma: 1). LMD diagnosed at HGG diagnosis (n=18) versus recurrence (n=22) was associated with longer post-LMD survival [pLMD-OS: 15.3m vs. 4.8m, HR: 0.07, 95% CI: 0.02-0.29, p=0.0004] but similar overall survival [mOS: 15.3m vs. 12.3m; HR: 0.82; 95% CI: 0.36-1.85; p=0.63]. Pathology-diagnosed LMD (n=15) versus MRI-diagnosed LMD (n=26) was associated with longer post-LMD survival [pLMD-OS: 15.4m vs. 5.2m, HR: 14.9, 95% CI: 0.01-0.30, p=0.0004] but similar overall survival [mOS: 17.1m vs. 12.3m; HR: 0.66; 95% CI: 0.3-1.58; p=0.38]. Post-LMD survival was significantly prolonged for supratentorial (n=28) versus infratentorial/spinal (n=4) locations regardless of the diagnostic modality [pLMD-OS: 2.6m vs. 11.3m, HR: 14.4, 95% CI: 2.73-75.7, p=0.0017], and did not significantly differ between symptomatic (n=20) and asymptomatic (n=23) patients [pLMD-OS: 4.8m vs. 11.2m, HR: 1.75, 95% CI: 0.82-3.77, p=0.15). *pTERT* mutation (81%), *EGFR* amplification (43%), and *MGMT* methylation (33%) were prevalent but *IDH1 mutation was rare (2.8%). Comparison with a separate glioblastoma cohort (n=1400) suggested more frequent amplification of CHIC2, MDM4, and KDR, higher mutation rates of RUNX1, APC, and RAD51C, colder tumor microenvironment (TME), and lower expression of immune checkpoint-related genes.* CONCLUSIONS: *Clinicopathological characteristics affect post-LMD survival, and cohort comparison suggests molecular and TME differences in LMD-HGG tumors.*

### PATH-23. HIGHLY INFILTRATING OLIGODENDROGLIOMAS SHOW DIFFERENT MORPHOLOGY FROM TYPICAL OLIGODENDROGLIOMAS WHILE MAINTAINING GOOD RESPONSE TO CHEMO-RADIATION THERAPY.

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Oligodendrogliomas are diffuse gliomas located in the cerebral hemisphere, and the MRI typically show swollen cortex and subcortical white matter by the tumor cells. IDH mutation and 1p/19q co-deletion define oligodendrogliomas in WHO classification, and these genetic alterations are associated with good response to chemo-radiation therapy and better prognosis compared to the IDH-mutant astrocytomas. We reviewed MRI findings of 60 oligodendrogliomas with 1p/19q co-deleted tumors which were diagnosed at Dokkyo Medical University since 1999. Of those, 3 cases showed highly infiltrating pattern in which tumors were more predominant in the white matter than the cortex and the infiltration involved multiple lobes. We retrospectively investigated those 3 cases for histological features, treatment, and clinical outcome. There were 2 males and 1 female. MRI showed faint-brushed Gd enhancement around the center of the tumor-infiltrated area in 1 case, while there was no enhancing lesion in other 2 cases. All three underwent stereotactic biopsy. Histologically, all 3 cases lacked typical oligodendroglioma morphology: the tumor cells have irregular round, oval to elongated nuclei without perinuclear halo and had dense, closed chromatin similar to astrocytoma. Two cases underwent chemotherapy (TMZ and PAV accordingly), without radiation and 1 case underwent chemotherapy with radiation as the primary treatment. Interestingly, all three tumors responded well not only to the primary treatments but also to the radiation therapy administered after recurrence, although all eventually succumbed to the tumor. PFS were 16, 37, 67 months and OS were 104, 70, 115 months for each, which were at the worse end as oligodendrogliomas but are apparently better than astrocytomas. Highly infiltrating oligodendrogliomas appeared to show significantly different MRI and histological features from typical oligodendrogliomas that primarily involve cerebral cortex. The underlying mechanism of such differences might involve specific genetic alterations and/or gene expression alterations that may not affect treatment response.

### PATH-24. ACCURATE IDENTIFICATION OF GLIAL MALIGNANCIES FROM PERIPHERAL BLOOD

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Symptomatic presentation of patients with intra-cranial malignancy is frequently non-specific and differentiating such patients from those with benign conditions is challenging. Accordingly, GBM presents as a medical emergency more frequently than any other common cancer, implying that effective strategies for rapid and simple diagnostic stratification of such patients are urgently required. Here we describe the detection of glial malignancies based on the enrichment and identification of Circulating Glial Cells (CGCs) in peripheral blood. The first case controlled study included blood from 189 participants split into discrete training and test sets (145 GBM, 44 benign CNS conditions). The second case controlled study included 40 cases of glial malignancies, 22 benign CNS conditions, 24 solid tumors with brain metastases, and 500 healthy individuals with no prior diagnosis of cancer and no current suspicion of cancer. A third prospective study was also carried out in 68 individuals with radiologically evident intracranial space-occupying lesion suspected of glial malignancies. Blood specimens were blindly evaluated for detection of CGCs through TruBlood assay to determine clinical sensitivity and specificity. 98% sensitivity and specificity was observed in detecting glial malignancies and differentiating them from benign CNS conditions in both case controlled studies. We detected and differentiated glial malignancies from benign CNS, healthy samples, and brain metastases. In the prospective study, 56 were positive for CGS, and 12 were negative for CGCs. All CGC positive specimens were confirmed glial malignancies and all CGC negative specimens benign CNS conditions. We present a non-invasive approach to the diagnostic stratification of patients presenting with suspicious but non-specific neurocognitive symptoms and hence early detection of glial malignancies. Moreover, immunocytochemistry facilitates the differentiation of GBM from metastatic intra-cranial epithelial cancers.

### PATH-25. LEPTOMENINGEAL, DURAL, AND EXTRACRANIAL METASTASIS OCCUR IN DIVERSE TYPES OF ADULT HIGH-GRADE GLIOMA

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BACKGROUND: Leptomeningeal and extracranial metastases in adult high-grade gliomas are being increasingly recognized as critical issues. Our group has a longstanding interest in this issue, having published multiple examples in 2015 (PMID: 26308254) and 1996 (8617464). We now update our experience, illustrating that dissemination can occur in diverse types of high-grade gliomas, even those with purportedly more favorable prognoses. METHODS: Search of records, 2018-present, to identify patients with leptomeningeal, dural, and/or extracranial spread clinically recognized prior to patient demise. RESULTS: Leptomeningeal dissemination was identified in 6 patients: one astrocytoma (frontal lobe, IDH1 R132H+, metastatic to 3-levels spinal cord), a second astrocytoma (frontal lobe, IDH1 R132H+, metastatic to spinal cord with intracranial dissemination), one glioblastoma, small cell type (*PIK3CA*, *CDH1*, *TP53* mutations, temporal lobe metastatic to cervical cord), one high-grade glioma with piloid features (HGAP, metastatic at presentation; *BRAF*-mutant, classified by DNA methylation (NIH)) and one high-grade glioma with no match to DNA methylation class (metastatic at presentation, NIH). There were three additional patients: one patient with glioblastoma with *FGFR*: *TACC3* fusion with short-interval dural and cervical lymph node metastases (in Press), one patient with glioblastoma with EGFR amplification and dural invasion and one patient with glioblastoma with massive dural spread and bony invasion at presentation. CONCLUSION: Although these new 9 individual cases provide no insights into the epidemiology of GBM leptomeningeal, dural and extracranial metastases, our single-institution series, using updated molecular classifications not always available in retrospective studies, shows that dissemination can occur in any, and all, types of adult high-grade gliomas. We put this cohort in perspective with our experience with dissemination in other low and high-grade tumor types: anaplastic myxopapillary ependymomas (30417460), H3 K27M-altered high-grade gliomas (29393845), pineal parenchymal tumors of intermediate differentiation (34418607), myxoid glioneuronal tumor, PDGFRA-mutant (34297434) and spinal cord gangliogliomas (25015869).

### PATH-26. COMPLEMENTARY CLASSIFICATION APPROACH TO RESOLVE LOW-SCORE RESULTS FROM THE DKFZ METHYLATION CLASSIFIER FOR CNS TUMOR DIAGNOSTICS

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DNA methylation-classification using the DKFZ CNS tumor classifier is highly useful, but experience indicates that approximately one-third of clinical cases do not reach the confidence threshold (0.84) for a definitive match. A low-confidence score can be observed for a variety of reasons, and addressing such instances is not always clear. We developed a complementary classification approach that differs from the DKFZ classifier